

SEQUENCE LISTING

<110> Daniel Cohen  
Ilya Chumakov

<120> TREATMENT OF CNS DISORDERS USING D-AMINO ACID OXIDASE AND D-ASPARTATE OXIDASE ANTAGONISTS

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413

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461

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509

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125 130 135

557

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140 145 150

605

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155 160 165 170

653

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175 180 185

701

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190 195 200

749

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205 210 215

797

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845

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88

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Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu  
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Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His  
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Ser Pro Asn Ala Gly Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn  
85 90 95  
Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys Asp Thr Val Leu  
100 105 110  
Gly Phe Arg Lys Leu Thr Pro Arg Gln Leu Asp Met Phe Pro Asp Tyr  
115 120 125  
Gly Tyr Gly Trp Phe His Thr Ser Leu Ile Leu Glu Gly Lys Asn Tyr  
130 135 140  
Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg Gly Val Lys Phe  
145 150 155 160  
Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg Glu Gly Ala Asp  
165 170 175  
Val Ile Val Asn Cys-Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp  
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Pro Leu Leu Gln Pro Gly Arg Gln Ile Met Lys Asp Pro Asp Ser  
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Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala  
35 40 45  
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Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Asp Val Ala  
35 40 45  
Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro Asn Asn Pro Gln Glu  
50 55 60  
Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu Leu Ser His Val His  
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Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn  
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Leu Phe His Glu Ala Ile Pro Val Ala Arg Glu Gly Ala Asp Val Ile  
100 105 110  
Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp Pro Leu  
115 120 125  
Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro Trp Met  
130 135 140  
Lys His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr Asn Ser  
145 150 155 160  
Pro Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly Ile Phe  
165 170 175  
Gln Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His Asn Thr  
180 185 190  
Ile Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn Ala Arg  
195 200 205  
Ile Ile Gly Glu Arg Thr Gly Phe Arg Pro Val Arg Pro Gln Ile Arg  
210 215 220  
Leu Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu Val Ile  
225 230 235 240  
His Asn Tyr Gly His Gly Gly Tyr Gly Leu Thr Ile His Trp Gly Cys  
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attaaaaatag ctgttaggat tactcatttt cttttttctt ctttttaaat ataaagcaat    180
gtcatcaattt tttccctgtt atttatatttc ttctcaataaa ttgatatgtt acattaaagg    240
aacacaaaat ggtcttaattt atgcaataat gatcaaggca aagagtgttt cttgggaact    300
aatggttgcc ttgagggagg ttatggcttg aggttccagct gggttattaag ccgcaggaaa    360
tgtgcagggc caaattttgtt atttttctc ttgatgtaaa atgaaacccaa aaaaaggcaa    420
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actcacacaa atcacctttt cctgtataca ttttttagat gtcaacatcc attctaatga   180
tttctcttag ttgcggccca aaattgtatt ctacrgtggtg attttaaagc tgaattttca  240
agatgtatatt tcatacttat attttcacaa gtttttcttc tatgaatgtt attgtcagct 300
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taagacaaag tcattactag gctgtaaaact gttgtctgc aaaattgagc agcacgtatt 420
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                           Met Leu Glu
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aag ctg atg ggt gct gat tmt ctc cag ctt ttc aga tcc aga tat aca      103
Lys Leu Met Gly Ala Asp Xaa Leu Gln Leu Phe Arg Ser Arg Tyr Thr
   5          10           15
ttg ggt aaa atc tac ttc ata ggt ttt caa arg agc att ctt ctg agc      151
Leu Gly Lys Ile Tyr Phe Ile Gly Phe Gln Xaa Ser Ile Leu Leu Ser
  20         25           30           35
aaa tct gaa aac tct cta aac tct att gca aag gag aca gaa kaa gga      199
Lys Ser Glu Asn Ser Leu Asn Ser Ile Ala Lys Glu Thr Glu Xaa Gly
   40         45           50
aga gag acg gta aca agg aaa gaa rga tgg aag aga agg cat gag gac      247
Arg Glu Thr Val Thr Arg Lys Glu Xaa Trp Lys Arg Arg His Glu Asp
   55         60           65
ggc tat ttg gaa atg gca cag agg cat tta cag aga tca tta tgt cct      295
Gly Tyr Leu Glu Met Ala Gln Arg His Leu Gln Arg Ser Leu Cys Pro
   70         75           80
tgg gtc tct tac ctt cct cag ccc tat gca gag ctt gaa gaa gta agc      343
Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu Glu Val Ser
   85         90           95
agc cat gtt gga aaa gtc ttc atg gca aga aac tat gag ttc ctt gmc      391
Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu Phe Leu Xaa
  100        105          110           115
tat gag gcc tct aar gac cgc agg cag cct cta gaa cga atg tgg acc      439
Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg Met Trp Thr

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120	125	130	
tgc aac tac aac cag caa aaa gac cag tca tgc aac cac aag gaa ata			487
Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His Lys Glu Ile			
135	140	145	
act tct acc aaa gct gaa tga gtttggaaac agattttcc cagccaatcc			538
Thr Ser Thr Lys Ala Glu *			
150			
ttctgtatgac aaatgtatgtc ggccaaacatc ttcaactggam tctgacggac tctgtgtctg			598
ggaccggact gataaacatcg gtgtatggg ttgtatattgc aaytctctgg tcagtaatgt			658
ataaaaatgcc atttctatgc acccacctgg cctgtgtgac tgggagaatyy tctttttta			718
ttaawtgttc ttcaagtttt aaca			742

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Leu Leu Ser Lys Ser Glu Asn Ser Leu Asn Ser Ile Ala Lys Glu Thr			
35	40	45	
Glu Xaa Gly Arg Glu Thr Val Thr Arg Lys Glu Xaa Trp Lys Arg Arg			
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His Glu Asp Gly Tyr Leu Glu Met Ala Gln Arg His Leu Gln Arg Ser			
65	70	75	80
Leu Cys Pro Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu			
85	90	95	
Glu Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu			
100	105	110	
Phe Leu Xaa Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg			
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Met Trp Thr Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His			
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tta tgt cct tgg gtc tct tac ctt cct cag ccc tat gca gag ctt gaa			96
Leu Cys Pro Trp Val Ser Tyr Leu Pro Gln Pro Tyr Ala Glu Leu Glu			
20	25	30	
gaa gta agc agc cat gtt gga aaa gtc ttc atg gca aga aac tat gag			144
Glu Val Ser Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu			
35	40	45	
tto ctt gcc tat gag gcc tct aag gac cgc agg cag cct cta gaa cga			192
Pho Leu Ala Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg			
50	55	60	
atg tgg acc tgc aac tac aac cag caa aaa gac cag tca tgc aac cac			240
Met Trp Thr Cys Asn Tyr Asn Gln Gln Lys Asp Gln Ser Cys Asn His			

65	70	75	80		
aag gaa ata act tct acc aaa gct gaa tga gtttggaaac agattttcc				290	
Lys Glu Ile Thr Ser Thr Lys Ala Glu *					
85	90				
cagccaaatcc ttctgtatgc aatgttagtc gcgcacatc ttcaactggac tctgacggac				350	
tctgtgtctg ggaccacgt gataaacacgt ggtgtatgggaa ttgtatggc aactctctgg				410	
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20                    25                    30					
Glu Val Ser His Val Gly Lys Val Phe Met Ala Arg Asn Tyr Glu					
35                    40                    45					
Phe Leu Ala Tyr Glu Ala Ser Lys Asp Arg Arg Gln Pro Leu Glu Arg					
50                    55                    60					
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ccccctcagga aatagcatcc tgggtccccg cactgcagtt gtctggcttc tccagcagtt					180
tggtaacttcc ggctgtctca atg cgt gtg gtg gtg att gga gca ggc gtc atc					233
Met Arg Val Val Ile Gly Ala Gly Val Ile					
1                    5                    10					
ggg ctg tcc acc gcc ctc tgc atc cat gag cgc tac cac tca gtc ctg					281
Gly Leu Ser Thr Ala Leu Cys Ile His Glu Arg Tyr His Ser Val Leu					
15                    20                    25					
cag cca ctg cac ata aag gtc tac ggc gac cgc ttc acc cca ctc acc					329
Gln Pro Leu His Ile Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr					
30                    35                    40					
acc acc gac gtg gct ggc ggc ctc tgg cag ccc tac tct tct gac ccc					377
Thr Thr Asp Val Ala Ala Gly Leu Trp Gln Pro Tyr Leu Ser Asp Pro					
45                    50                    55					
aac aac cca cag gag ggc gac tgg agc caa cag acc ttt gac tat ctc					425
Asn Asn Pro Gln Glu Ala Asp Trp Ser Gln Gln Thr Phe Asp Tyr Leu					
60                    65                    70                    75					
ctg agc cat gtc cat tct ccc aac gct gaa aac ctg ggc ctg ttc cta					473
Leu Ser His Val His Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu					
80                    85                    90					
atc tcg ggc tac aac ctc ttc cat gaa gcc att ccg gac cct tcc tgg					521
Ile Ser Gly Tyr Asn Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp					
95                    100                    105					
aag gac aca gtt ctg gga ttt cgg aag ctg acc ccc aga gag ctg gat					569

Lys	Asp	Thr	Val	Leu	Gly	Phe	Arg	Lys	Leu	Thr	Pro	Arg	Glu	Leu	Asp	
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Met	Pho	Pro	Asp	Tyr	Gly	Tyr	Gly	Tyr	Trp	Pho	His	Thr	Ser	Leu	Ile	Leu
125						130					135					135
gag	gga	aag	aac	tat	cta	cag	tgg	ctg	act	gaa	agg	tta	act	gag	agg	665
Glu	Gly	Lys	Asn	Tyr	Leu	Gln	Trp	Leu	Thr	Glu	Arg	Leu	Thr	Glu	Arg	
140						145					150					155
gga	gtg	aag	ttc	ttc	cag	cgg	aaa	gtg	gag	tct	ttt	gag	gag	gtg	gca	713
Gly	Val	Lys	Phe	Phe	Gln	Arg	Lys	Val	Glu	Ser	Phe	Glu	Glu	Val	Ala	
						160					165					170
aga	gaa	ggc	gca	gac	gtg	att	gtc	aac	tgc	act	ggg	gta	tgg	gct	ggg	761
Arg	Glu	Gly	Ala	Asp	Val	Ile	Val	Asn	Cys	Thr	Gly	Val	Trp	Ala	Gly	
						175					180					185
gcg	cta	caa	cga	gac	ccc	ctg	ctg	cag	cca	ggc	cgg	ggg	cag	atc	atg	809
Ala	Leu	Lys	Arg	Asp	Pro	Leu	Leu	Gln	Pro	Gly	Arg	Gly	Gln	Ile	Met	
						190					195					200
aag	gtg	gac	gcc	cct	tgg	atg	aag	cac	ttc	att	ctc	acc	cat	gac	cca	857
Lys	Val	Asp	Ala	Pro	Trp	Met	Lys	His	Phe	Ile	Leu	Thr	His	Asp	Pro	
						205					210					215
gag	aga	ggc	atc	tac	aat	tcc	ccg	tac	atc	atc	cca	ggg	acc	cag	aca	905
Glu	Arg	Gly	Ile	Tyr	Asn	Ser	Pro	Tyr	Ile	Ile	Pro	Gly	Thr	Gln	Thr	
						220					225					235
gtt	act	ctt	gga	ggc	atc	ttc	cag	tgg	gga	aac	tgg	agt	gaa	cta	aac	953
Val	Thr	Leu	Gly	Gly	Ile	Phe	Gln	Ieu	Gly	Asn	Trp	Ser	Glu	Leu	Asn	
						240					245					250
aat	atc	cag	gac	cac	acc	att	tgg	gaa	ggc	tgc	aga	ctg	gag			1001
Asn	Ile	Gln	Asp	His	Asn	Thr	Ile	Trp	Glu	Gly	Cys	Arg	Leu	Glu		
						255					260					265
ccc	aca	ctg	aat	gca	aga	att	at	gtt	gaa	gca	act	ggc	tcc	cg		1049
Pro	Thr	Leu	Lys	Asn	Ala	Arg	Ile	Ile	Gly	Glu	Ala	Thr	Gly			
						270					275					280
cct	tca	aaa	aca	aca	gag	gtc	atc	cac	aac	att	ttt	ggc	cat	gga	ggc	1145
Pro	Ser	Asn	Thr	Glu	Val	Ile	His	Asn	Tyr	Gly	His	Gly	Gly	Tyr	Gly	
						285					290					295
cct	tca	aaa	aca	aca	gag	gtc	atc	cac	aac	ttt	ggc	cat	gga	ggc		1097
Leu	Thr	Ile	His	Trp	Gly	Cys	Ala	Leu	Glu	Ala	Ala	Lys	Leu	Phe	Gly	
						300					305					310
cct	acc	acc	cac	tcc	ggg	tgt	gcc	ctg	gag	gca	gcc	aag	ctc	ttt	ggg	1193
Leu	Thr	Ile	His	Trp	Gly	Cys	Ala	Leu	Glu	Ala	Ala	Lys	Leu	Phe	Gly	
						320					325					330
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Arg	Ile	Leu	Glu	Glu	Lys	Lys	Leu	Ser	Arg	Met	Pro	Pro	Ser	His	Leu	
						335					340					345
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 Lys Val Tyr Ala Asp Arg Phe Thr Pro Leu Thr Thr Thr Asp Val Ala  
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 Ser Pro Asn Ala Glu Asn Leu Gly Leu Phe Leu Ile Ser Gly Tyr Asn  
 85 90 95  
 Leu Phe His Glu Ala Ile Pro Asp Pro Ser Trp Lys Asp Thr Val Leu  
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 Gly Phe Arg Lys Leu Thr Pro Arg Glu Leu Asp Met Phe Pro Asp Tyr  
 115 120 125  
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 130 135 140  
 Leu Gln Trp Leu Thr Glu Arg Leu Thr Glu Arg Gly Val Lys Phe Phe  
 145 150 155 160  
 Gln Arg Lys Val Glu Ser Phe Glu Glu Val Ala Arg Glu Gly Ala Asp  
 165 170 175  
 Val Ile Val Asn Cys Thr Gly Val Trp Ala Gly Ala Leu Gln Arg Asp  
 180 185 190  
 Pro Leu Leu Gln Pro Gly Arg Gly Gln Ile Met Lys Val Asp Ala Pro  
 195 200 205  
 Trp Met Lys His Phe Ile Leu Thr His Asp Pro Glu Arg Gly Ile Tyr  
 210 215 220  
 Asn Ser Pro Tyr Ile Ile Pro Gly Thr Gln Thr Val Thr Leu Gly Gly  
 225 230 235 240  
 Ile Phe Gln Leu Gly Asn Trp Ser Glu Leu Asn Asn Ile Gln Asp His  
 245 250 255  
 Asn Thr Ile Trp Glu Gly Cys Cys Arg Leu Glu Pro Thr Leu Lys Asn  
 260 265 270  
 Ala Arg Ile Ile Gly Glu Ala Thr Gly Phe Arg Pro Val Arg Pro Gln  
 275 280 285  
 Ile Arg Leu Glu Arg Glu Gln Leu Arg Thr Gly Pro Ser Asn Thr Glu  
 290 295 300  
 Val Ile His Asn Tyr Gly His Gly Gly Tyr Gly Leu Thr Ile His Trp  
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 tcc acg gct gtg tgc atc tcc aaa ctg gtg ccc cga tgc tcc gtt acc  
 Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr  
 20 25 30  
 atc att tca gac aag ttt act cca gat acc acc agt gat gtg gca gcc  
 Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala

48

96

144

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Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln			
50 55 60			
aag cag tgg ttc aga gaa acc ttt aat cac ctc ttt gca att gcc aat			240
Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn			
65 70 75 80			
tct gca gaa gct gga gat gct ggt gtc cat ttg gta tca ggt tgg cag			288
Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Trp Gln			
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Ile Phe Gln Ser Thr Pro Thr Glu Glu Val Pro Phe Trp Ala Asp Val			
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Val Leu Gly Phe Arg Lys Met Thr Glu Ala Glu Leu Lys Lys Phe Pro			
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Gln Tyr Val Phe Gly Gln Ala Phe Thr Thr Leu Lys Cys Glu Cys Pro			
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Ala Tyr Leu Pro Trp Leu Glu Lys Arg Ile Lys Gly Ser Gly Gly Trp			
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Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu Leu His Pro Ser Phe			
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Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser Arg Gln Leu Ala Gly			
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Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val Leu Gln Val Gln Ala			
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Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser Gly Leu Thr Tyr Ile			
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Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly Thr Arg Gln Lys Gly			
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Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser Arg Glu Ile Leu Ser			
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Glu Lys Val Gly Leu Arg Pro Tyr Arg Pro Gly Val Arg Leu Gln Thr			
275 280 285			
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Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro Val Val His His Tyr			
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Gly His Gly Ser Gly Ile Ser Val His Trp Gly Thr Ala Leu Glu			
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Ala Ala Arg Leu Val Ser Glu Cys Val His Ala Leu Arg Thr Pro Ile			
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Pro Lys Ser Asn Leu *			
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 Ser Thr Ala Val Cys Ile Ser Lys Leu Val Pro Arg Cys Ser Val Thr  
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 Ile Ile Ser Asp Lys Phe Thr Pro Asp Thr Thr Ser Asp Val Ala Ala  
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 Gly Met Leu Ile Pro His Thr Tyr Pro Asp Thr Pro Ile His Thr Gln  
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 Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Ile Lys  
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 Gly Ser Gly Trp Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu  
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 Leu His Pro Ser Phe Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser  
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 Arg Gln Leu Ala Gly Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val  
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Gly	Thr	Ala	Leu	Glu	Ala	Ala	Arg	Leu	Val	Ser	Glu	Cys	Val	His	Ala	
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Lys	Gln	Trp	Phe	Arg	Glu	Thr	Phe	Asn	His	Leu	Phe	Ala	Ile	Ala	Asn	
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Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly Thr Arg Gln Lys Gly		
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Lys Gln Trp Phe Arg Glu Thr Phe Asn His Leu Phe Ala Ile Ala Asn		
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Ser Ala Glu Ala Gly Asp Ala Gly Val His Leu Val Ser Gly Ile Lys		
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Gly Ser Gly Gly Trp Thr Leu Thr Arg Arg Ile Glu Asp Leu Trp Glu		
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Leu His Pro Ser Phe Asp Ile Val Val Asn Cys Ser Gly Leu Gly Ser		
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Arg Gln Leu Ala Gly Asp Ser Lys Ile Phe Pro Val Arg Gly Gln Val		
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Leu Gln Val Gln Ala Pro Trp Val Glu His Phe Ile Arg Asp Gly Ser		
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Gly Leu Thr Tyr Ile Tyr Pro Gly Thr Ser His Val Thr Leu Gly Gly		
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Thr Arg Gln Lys Gly Asp Trp Asn Leu Ser Pro Asp Ala Glu Asn Ser		
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Arg Glu Ile Leu Ser Arg Cys Cys Ala Leu Glu Pro Ser Leu His Gly		
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210	215	220
Val Arg Leu Gln Thr Glu Leu Leu Ala Arg Asp Gly Gln Arg Leu Pro		
225	230	235
240		
Val Val His His Tyr Gly His Gly Ser Gly Gly Ile Ser Val His Trp		

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47

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